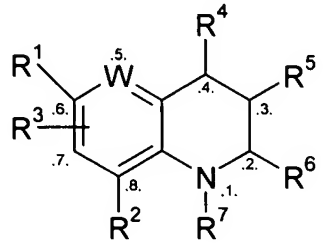
Patent Claims

1. Compounds of the formula I



I

in which

W denotes CH or N,

R^1, R^2, R^3, independently of one another, denote H, R, A, aryl, heteroaryl, Hal, $-(CY_2)_n-SA$, $-(CY_2)_n-SCF_3$, $-(CY_2)_n-SCN$, $-(CY_2)_n-CF_3$, $-(CY_2)_n-OCF_3$, cycloalkyl, $-SCH_3$, -SCN, $-CF_3$, $-OCF_3$, -OA, $-(CY_2)_n-OH$, $-(CY_2)_n-CO_2R$, $-(CY_2)_n-CN$, $-(CY_2)_n-Hal$, $-(CY_2)_n-NR_2$, $(CY_2)_n-OA$, $(CY_2)_n-OCOA$, $-SCF_3$, $(CY_2)_n-CONR_2$, $-(CY_2)_n-NHCOA$, $-(CY_2)_n-NHSO_2A$, SF_5, $Si(CH_3)_3$, $CO-(CY_2)_n-CH_3$, $-(CY_2)_n-N$-pyrrolidone, $CH(CH_2)_nNRCOOR$, CHNRCOOR, NCO, $CH(CH_2)_nCOOR$, NCOOR, $CH(CH_2)_nOH$, $N(CH_2)_nOH$, $CHNH_2$, $CH(CH_2)_nNR_2$, $CH(CH_2)_nNR_2$, C(OH)R, CHNCOR, $CH(CH_2)_n$-aryl, $CH(CH_2)_n$--heteroaryl, $CH(CH_2)_nR^1$, $N(CH_2)_nCOOR$, $CH(CH_2)_nX(CH_2)_n$-aryl, $CH(CH_2)_nX(CH_2)_n$-heteroaryl, $N(CH_2)_nCONR_2$, $XCONR(CH_2)_nNR_2$, $N[(CH_2)_nXCOOR]CO(CH_2)_n$-aryl, $N[(CH_2)_nXR]CO(CH_2)_n$-aryl, $N[(CH_2)_nXR]CO(CH_2)_nX$-aryl, $N[(CH_2)_nXR]SO_2(CH_2)_n$-aryl, $N[(CH_2)_nNRCOOR]CO(CH_2)_n$-aryl, $N[(CH_2)_nNR_2]CO(CH_2)_n$-aryl, $N[(CH_2)_nNR_2]CO(CH_2)_nNR$-aryl, $N[(CH_2)_nNR_2]SO_2(CH_2)_n$-aryl, $N[(CH_2)_nXR]CO(CH_2)_n$-

heteroaryl, $N[(CH_2)_nXR]CO(CH_2)_nX$-heteroaryl, $N[(CH_2)_nXR]SO_2(CH_2)_n$-heteroaryl, $N[(CH_2)_nNRCOOR]CO(CH_2)_n$-heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_n$-heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_nNR$-heteroaryl, $N[(CH_2)_nNR_2]SO_2(CH_2)_n$-heteroaryl, $O(CH_2)_nNR_2$, $X(CH_2)_nNR_2$, $NCO(CH_2)_nNR_2$, R^1 and R^2 together also denote -N-C(CF_3)=N-, -N-CR=N-, -N-N=N-,

Y denotes H, A, Hal

A denotes alkyl or cycloalkyl, in which one or more H atoms may be replaced by Hal,

Hal denotes F, Cl, Br or I,

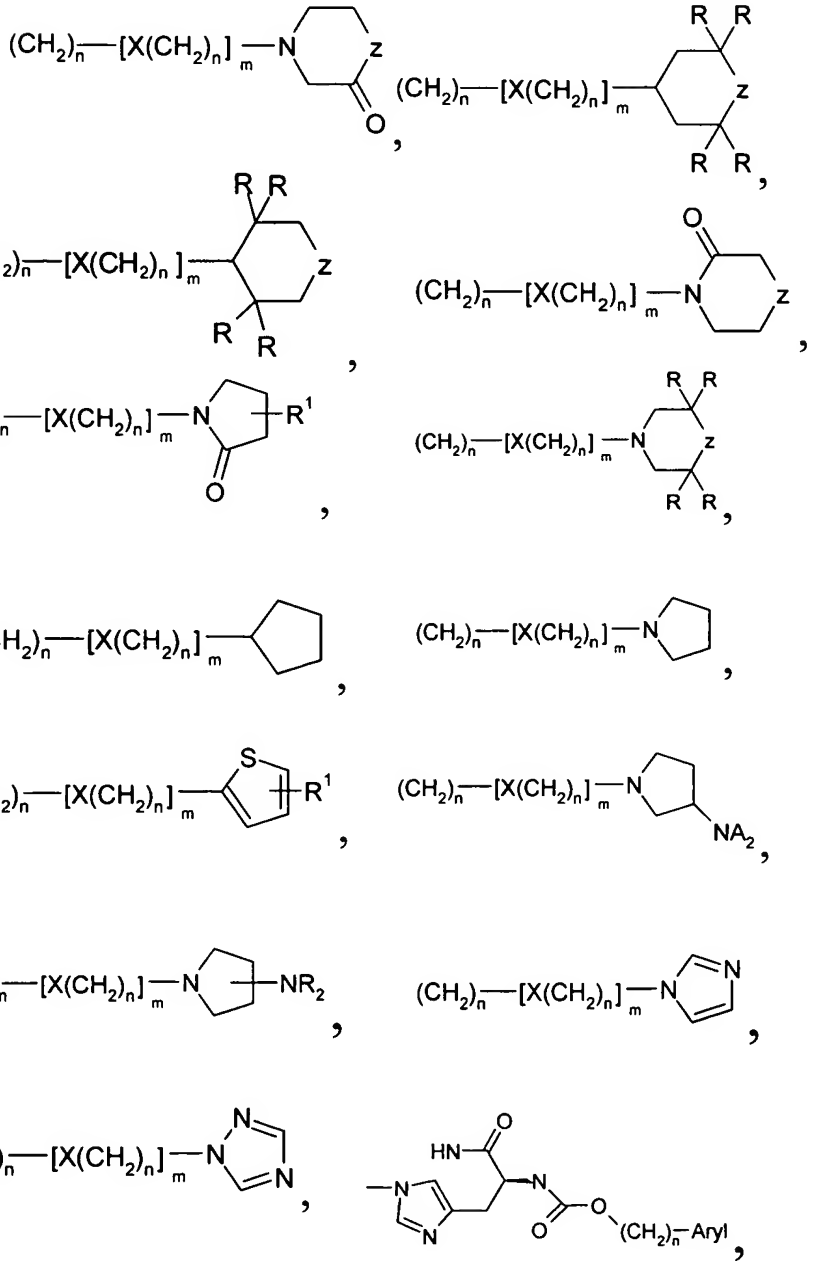
R denotes H or A, in the case of geminal radicals R together also $-(CH_2)_5$-, $-(CH_2)_4$-, $-(CH_2)_2$-X-$(CH_2)_2$ or $-(CH_2)_2$-Z-$(CH_2)_n$,

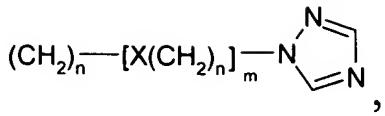
R^4, R^5, independently of one another, denote H or an unsubstituted or mono- or poly-OR-, NO_2-, Hal-, CF_3-, OCF_3-, CN-, NR_2- or SR-, aryl- or heteroaryl-substituted N-pyrrolidone radical, -X-$(CH_2)_2$OR, -X-$CO(CH_2)_nCH_3$, -X-$(CH_2)_2NR_2$, R^1, S-aryl, O-aryl, $CH_2Si(CH_3)_3$, or together denote -X$(CR_2)_2$-, -X-$(CR_2)_3$-, -X-$(CHCH_2OR)(CH_2)_2$-, -X-$(CHCH_2NR_2)(CH_2)_2$-, -X$(CH_2)_2NR_2$, -$(CR_2)_3$ -, -$(CR_2)_4$-,-CR=CR-CR=CR-, -XCHQ$(CR_2)_2$-, -XCHQCR_2-, R-N-(C=X)-N-R, -XC[(CH_2)nOR]$_2CH_2CH_2$-,

X denotes O, S or NR

Q denotes CH_2Hal, CHO, COR^a, CH_2R^a, CH_2OCOR^a, CH_2NCOR^1, $CH_2N(R^1)_2$, CH_2OR^1, $CH_2OCON(R^1)_2$, CH_2OCOOR^1, $CH_2NHCON(R^1)_2$, $CH_2NHCOOR^1$,

R^a denotes

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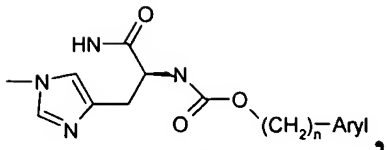
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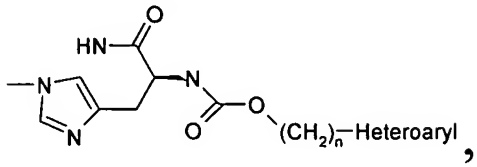
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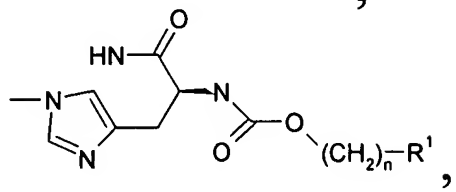
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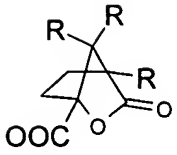
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OR, NHR_2, NR_2, $NR(CH_2)_n$-aryl, $NR(CH_2)_nOR$, COOR, N-pyrrolidone radical, OCOR, $NR(CH_2)_nNR_2$, $N[(CH_2)_nNR_2]CO(CH_2)_n$-aryl, $N[(CH_2)_nNHCOOR]CO$-aryl, R^1, $N[CH_2(CH_2)_nOR]_2$, $NR(CH_2)_nNCOOR$, $X(CH_2)_nX(CH_2)_nXR$, $NR(CH_2)_nX(CH_2)_nOH$, $NR(CH_2)_nO(CH_2)_nOH$, $(CH_2)_nCOOR$, $O(CO)NR(CH_2)_nOR$, $O(CO)(CH_2)_nNR_2$, $NR(CH_2)_nNR_2$, $N[(CH_2)_nNR_2]CO(CH_2)_n$-aryl, $N[(CH_2)_nXR]CO(CH_2)_n$-aryl, $N[(CH_2)_nXR]CO(CH_2)_n$-heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_n$-heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_nR^1$, $N(R)(CH_2)_nN(R)COOR$, $XCOO(CH_2)_nNR_2$, OSO_2A, OSO_2CF_3, OSO_2Ar, $OCONR_2$, $OCH_2(CH_2)_nNR_2$

Z denotes CH_2, X, $CHCONH_2$, $CH(CH_2)_nNRCOOR$, CHNRCOOR, NCO, $CH(CH_2)_nCOOR$, NCOOR, $CH(CH_2)_nOH$, $N(CH_2)_nOH$, $CHNH_2$, $CH(CH_2)_nNR_2$, $CH(CH_2)_nNR_2$, C(OH)R, CHNCOR, $CH(CH_2)_n$-aryl, $CH(CH_2)_n$-heteroaryl, $CH(CH_2)_nR^1$, $N(CH_2)_nCOOR$, $CH(CH_2)_nX(CH_2)_n$-aryl, $CH(CH_2)_nX(CH_2)_n$-heteroaryl, $N(CH_2)_nCONR_2$, $XCONR(CH_2)_nNR_2$, $N[(CH_2)_nXCOOR]CO(CH_2)_n$-aryl, $N[(CH_2)_nXR]CO(CH_2)_n$-

aryl, $N[(CH_2)_nXR]CO(CH_2)_nX$-aryl, $N[(CH_2)_nXR]SO_2(CH_2)_n$-aryl, $N[(CH_2)_nNRCOOR]CO(CH_2)_n$-aryl, $N[(CH_2)_nNR_2]CO(CH_2)_n$-aryl, $N[(CH_2)_nNR_2]CO(CH_2)_nNR$-aryl, $N[(CH_2)_nNR_2]SO_2(CH_2)_n$-aryl, $N[(CH_2)_nXR]CO(CH_2)_n$-heteroaryl, $N[(CH_2)_nXR]CO(CH_2)_nX$-heteroaryl, $N[(CH_2)_nXR]SO_2(CH_2)_n$-heteroaryl, $N[(CH_2)_nNRCOOR]CO(CH_2)_n$-heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_n$-heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_nNR$-heteroaryl, $N[(CH_2)_nNR_2]SO_2(CH_2)_n$-heteroaryl, $O(CH_2)_nNR_2$, $X(CH_2)_nNR_2$, $NCO(CH_2)_nNR_2$,

R^6 denotes aryl or heteroaryl, each of which is unsubstituted or mono- or polysubstituted by aryl or heteroaryl, each of which may be substituted by Hal, NO_2, CN, A, OR, OCOR, COR, NR_2, CF_3, OCF_3, $OCH(CF_3)_2$, or by Hal, NO_2, CN, OR, A, $-(CY_2)_n$-OR, -OCOR, $-(CY_2)_n-CO_2R$, $-(CY_2)_n$-CN, -NCOR, -COR or $-(CY_2)_n-NR_2$,

R^7 denotes (C=O)-R, (C=O)-NR_2, (C=O)-OR, H or A

m denotes 0, 1 or 2

and

n denotes 0, 1, 2, 3, 4, 5, 6 or 7,

and pharmaceutically usable derivatives, solvates, tautomers, salts and stereoisomers thereof, including mixtures thereof in all ratios.

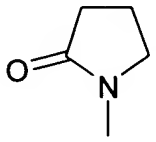
2. Compounds according to Claim 1 in which

R^1 denotes A, CF_3, OCF_3, SA, SCN, CH_2CN, -OCOA, Hal, SCF_3, t-butyl, $-CH(CH_3)CH_2CH_3$, isopropyl, ethyl or methyl.

3. Compounds according to Claim 1 or 2 in which
R^2 denotes denotes F or H.

4. Compounds according to one or more of Claims 1-3 in which
R^3 denotes F or H.

5. Compounds according to one or more of Claims 1-4 in which
R^4 preferably denotes one of the following groups if R^5 denotes H:

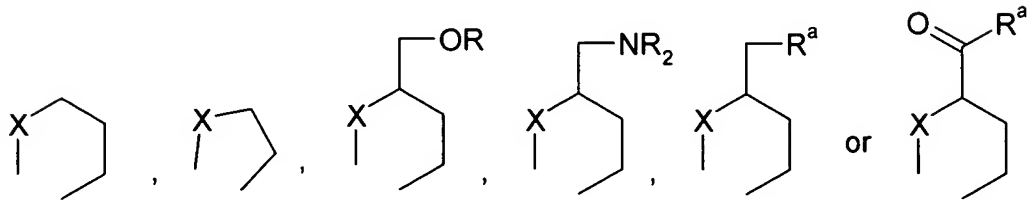


or $-X-(CH_2)_2-NR_2$

X and R have the meaning indicated in Claim 1.

6. Compounds according to one or more of Claims 1-5 in which
R^5 denotes H.

7. Compounds according to one or more of Claims 1-6 in which
R^5, together with R^4, adopts one of the following meanings:



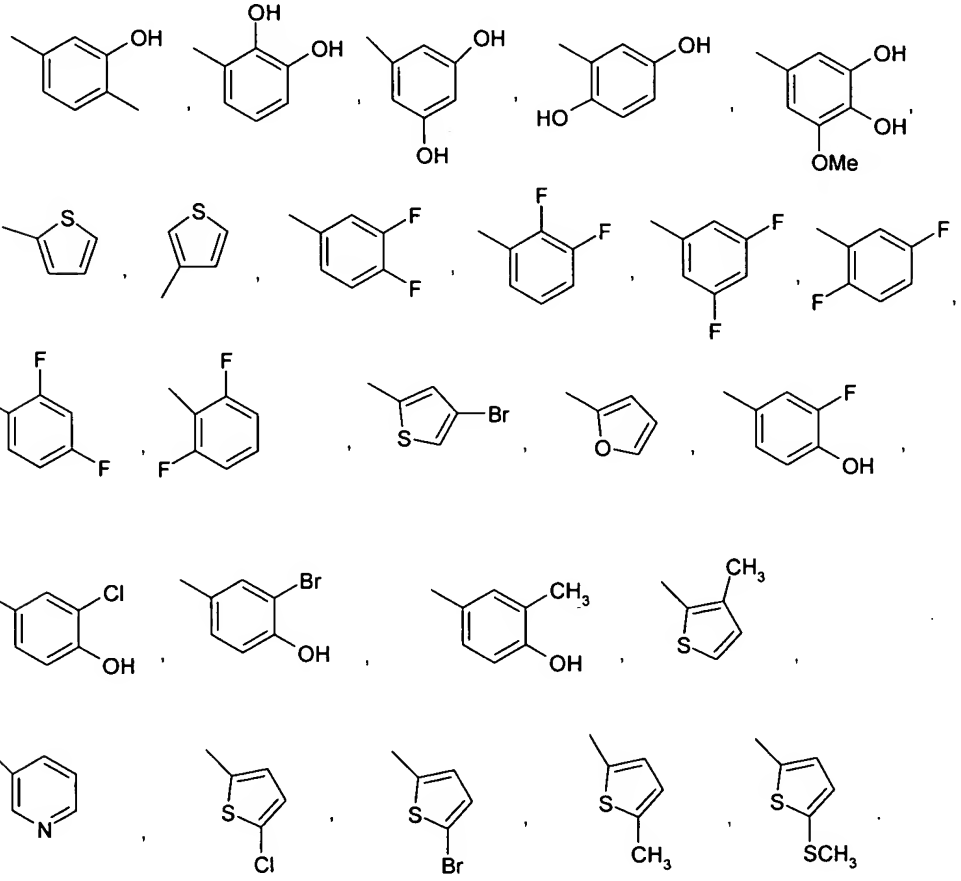
in which
X, R and R^a have the meaning indicated in Claim 1.

8. Compounds according to one or more of Claims 1-7 in which

R^6 denotes phenyl, 2-, 3- or 4-pyridyl, pyrimidyl, furyl or thienyl, each of which is unsubstituted or mono- or poly-substituted by Hal, CN, NO_2, OH, CF_3, $OCH(CF_3)_2$, $OCOCH_3$ or A.

9. Compounds according to one or more of Claims 1-8 in which

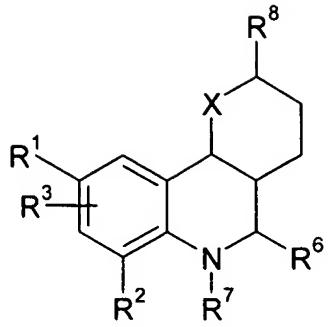
R^6 denotes one of the following groups:



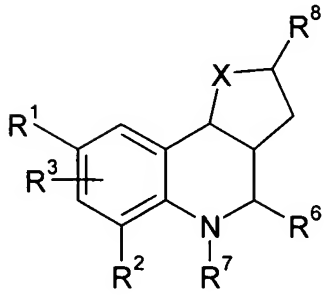
10. Compounds according to one or more of Claims 1-9 in which

R^7 denotes H.

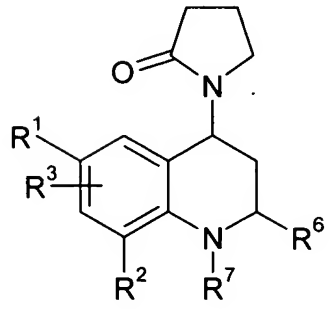
11. Compounds of the sub-formulae IA to ID:



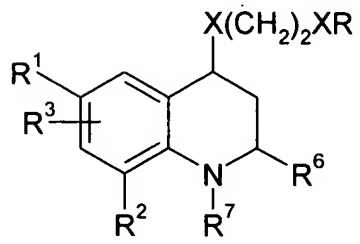
IA



IB



IC



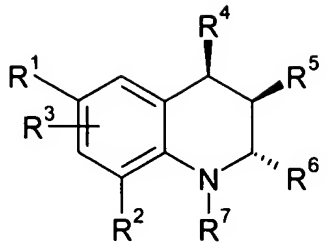
ID

in which R, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and X have the meaning indicated in Claim 1

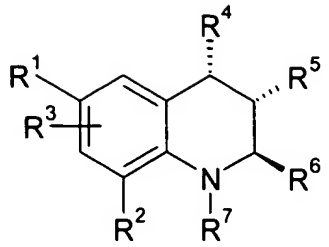
and

R^8 denotes H, CH_2OR or CH_2NR_2.

12. Compounds of the sub-formulae A and B:



A

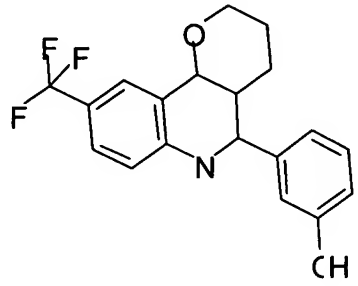


B

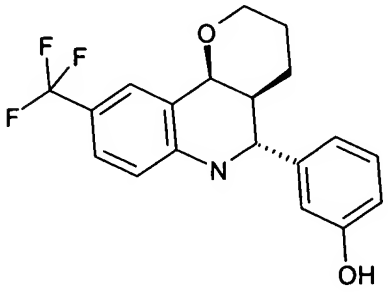
in which R^1, R^2, R^3, R^4, R^5, R^6, R^7 have the meaning indicated in Claim 1, and the racemate thereof or other mixtures of the enantiomers.

13. Compounds of the sub-formulae I1 to I45a:

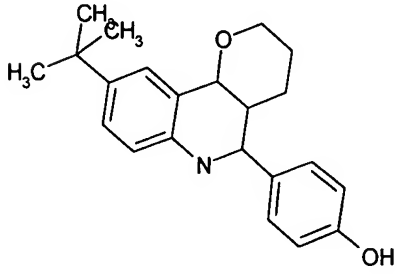
I1



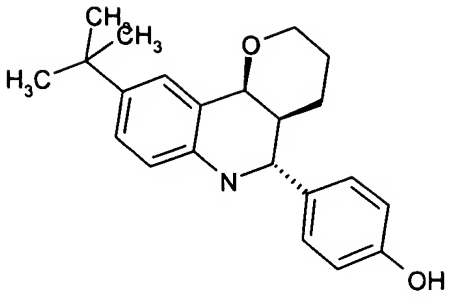
I1a



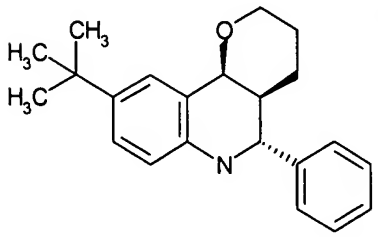
I2



I2a

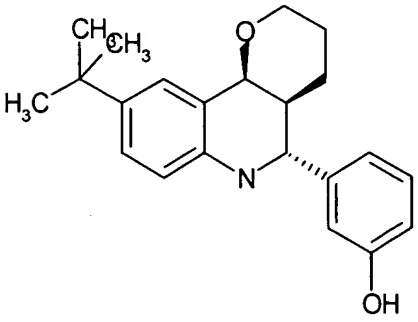


I3

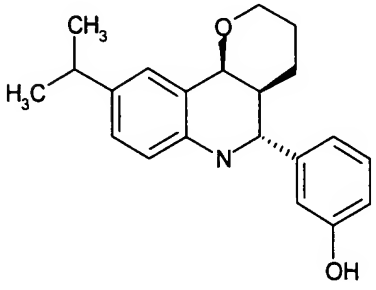


Chiral

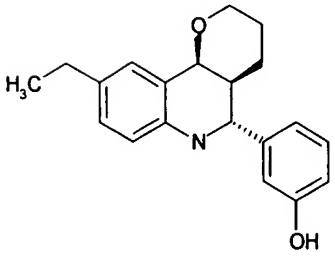
I4



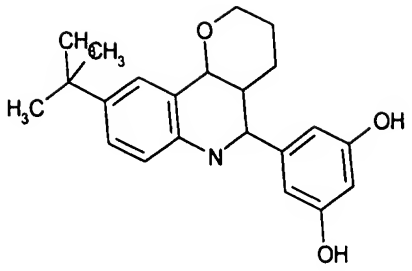
I5



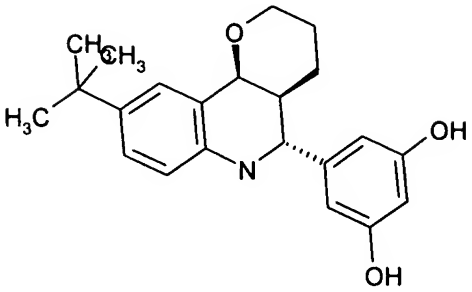
I6



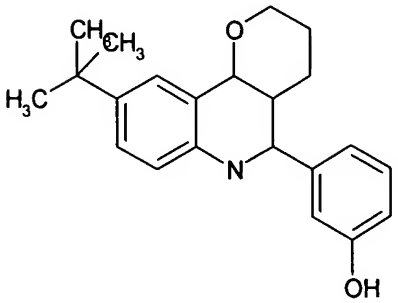
I7



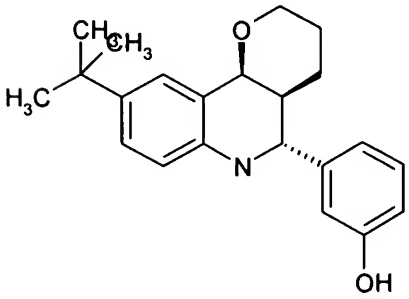
I7a



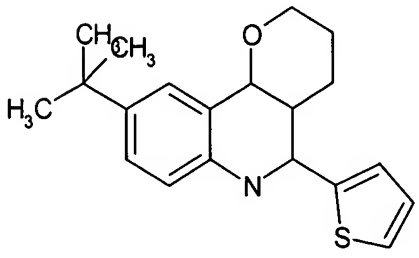
I8



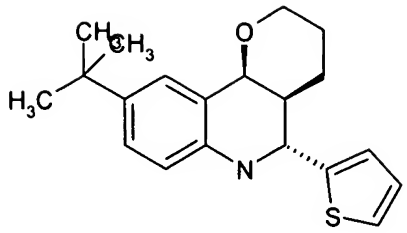
I8a



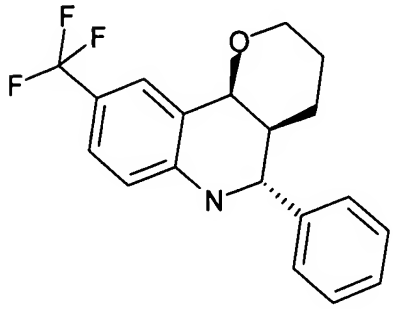
I9



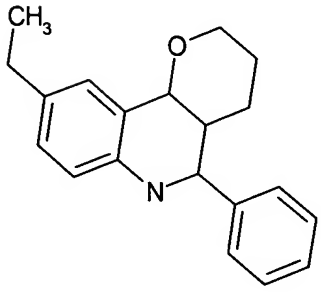
I9a



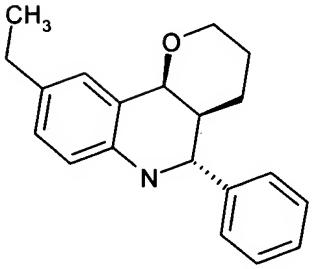
I10



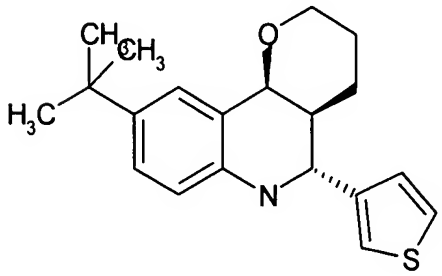
I11



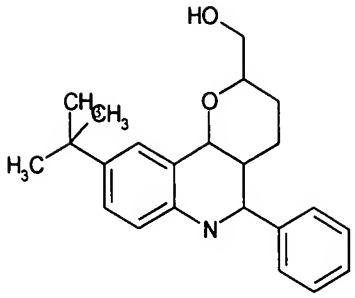
I11a



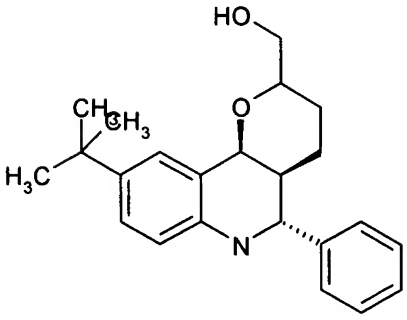
I12



I13



I13a



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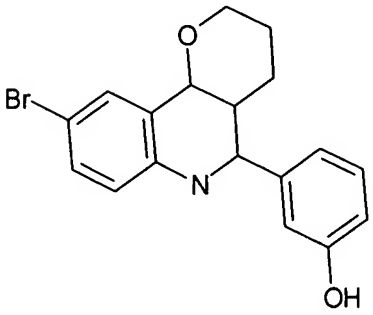

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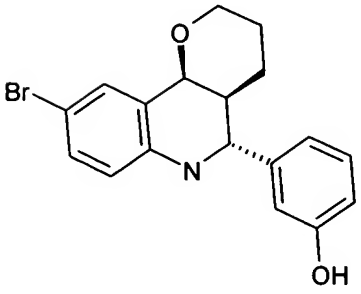

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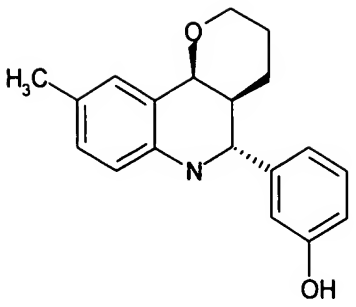

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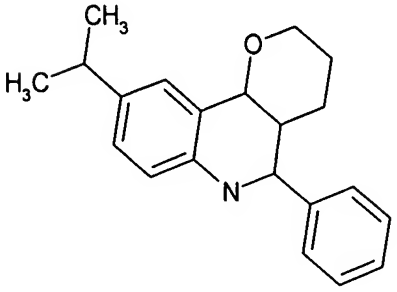

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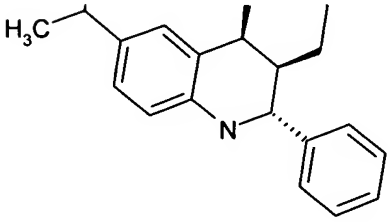

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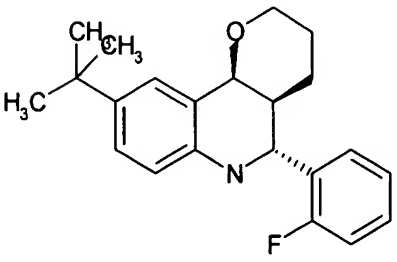

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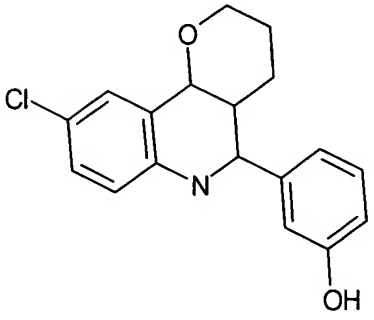

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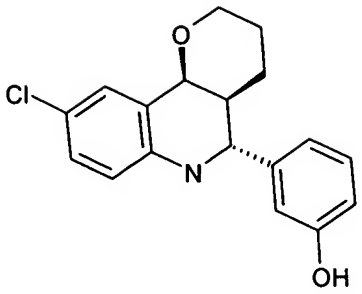

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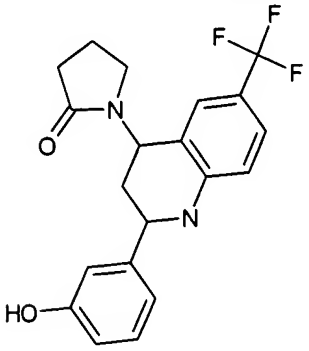

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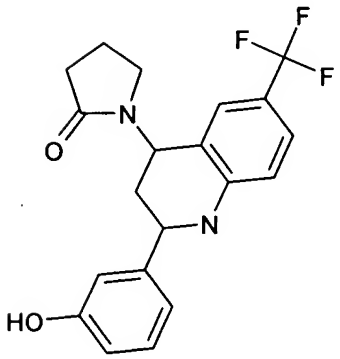

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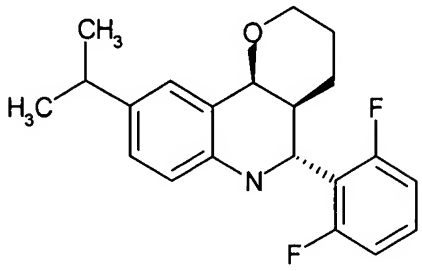

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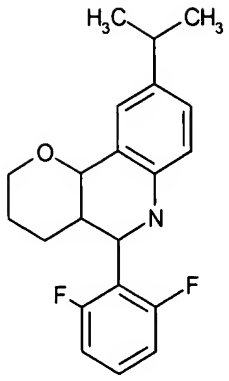

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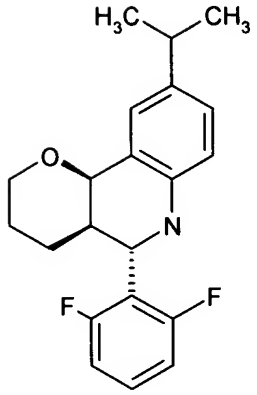

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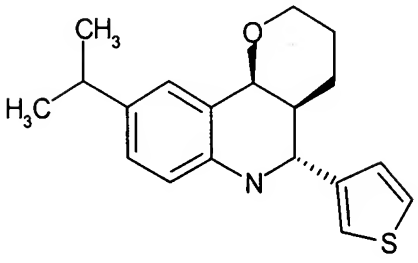

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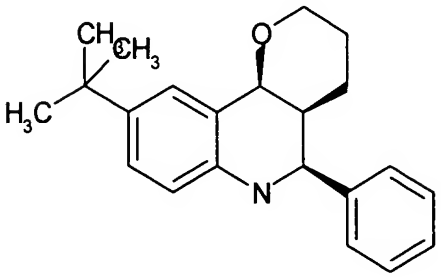

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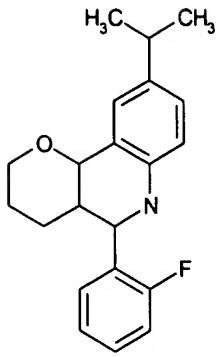

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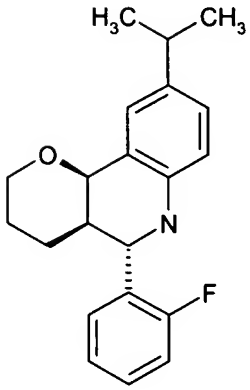

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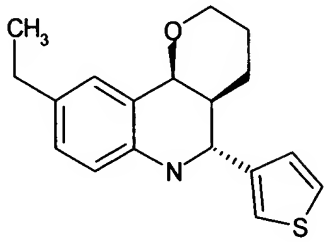

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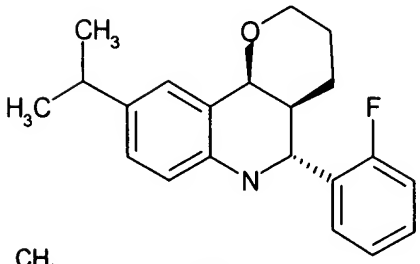

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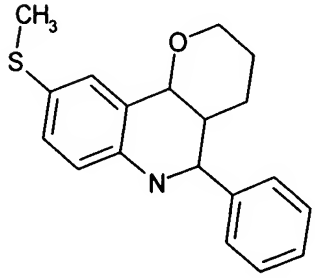

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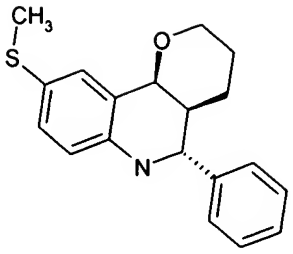

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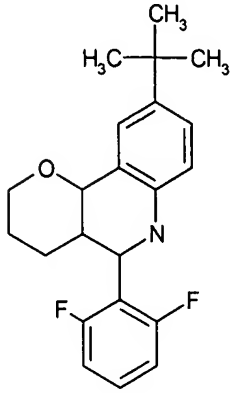

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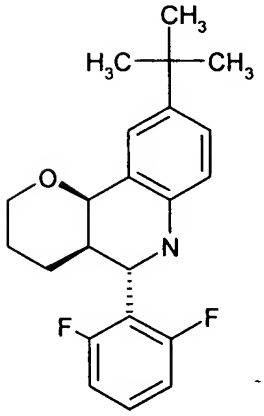

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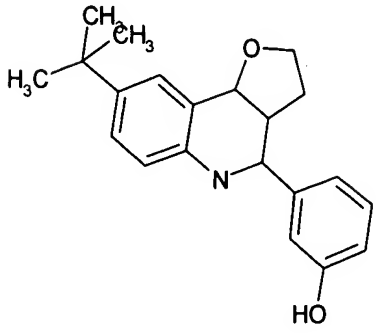

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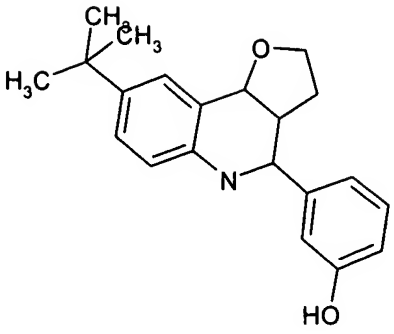

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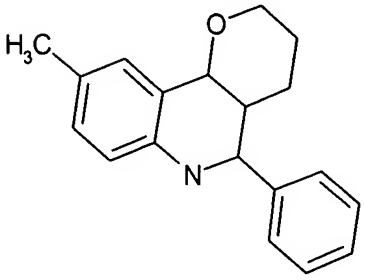

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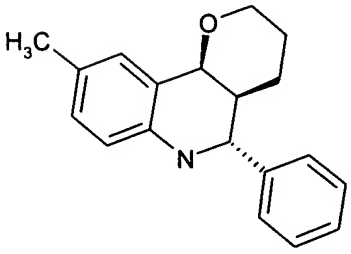

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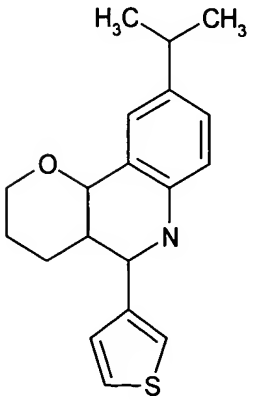

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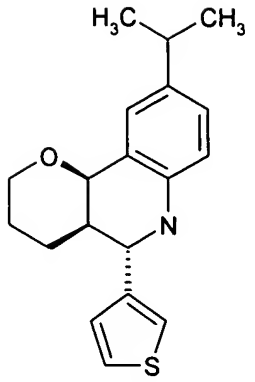

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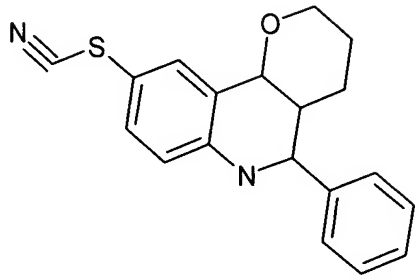

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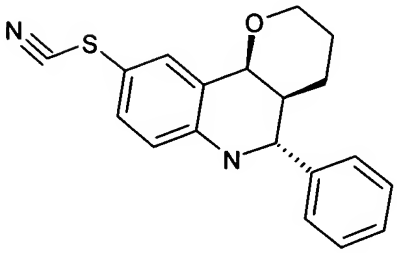

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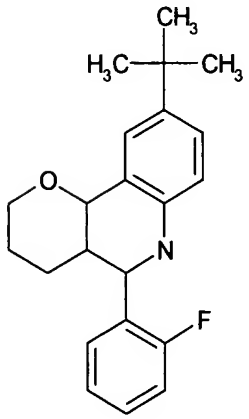

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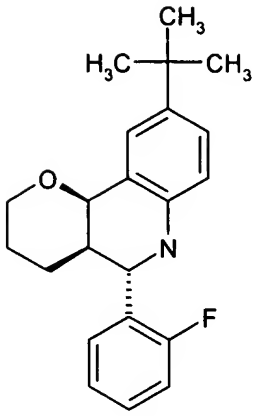

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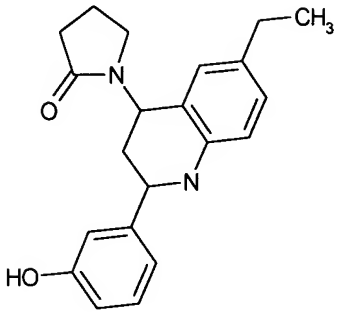

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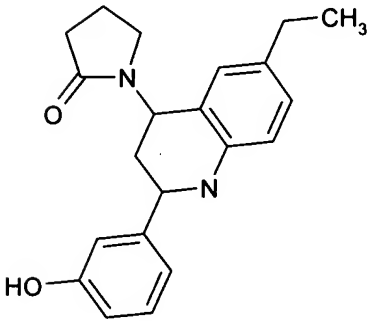

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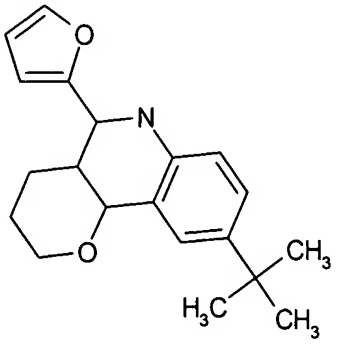

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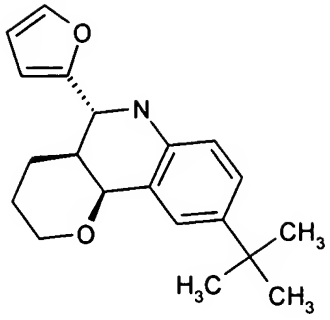

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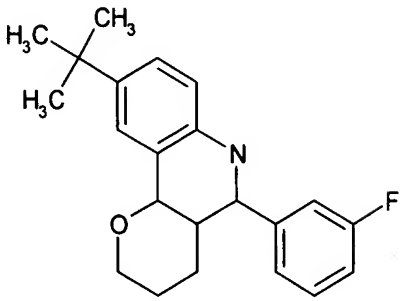

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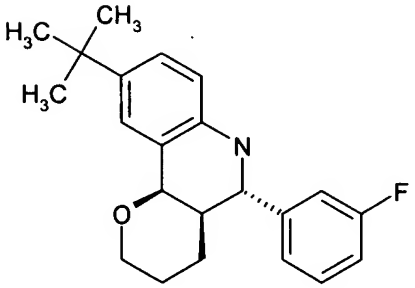

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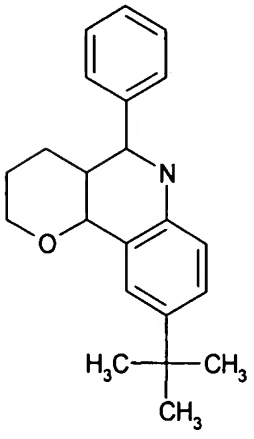

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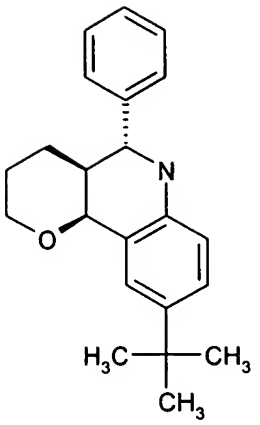

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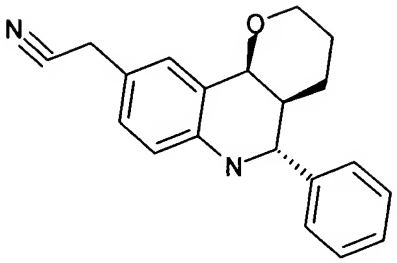

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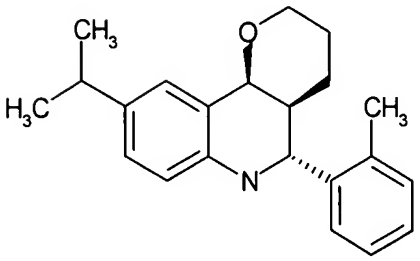

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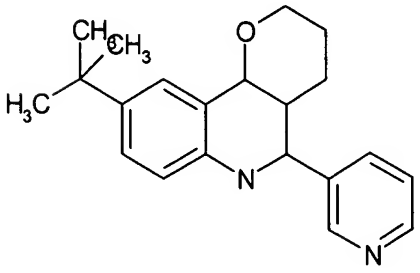

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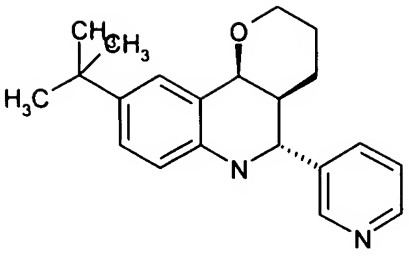

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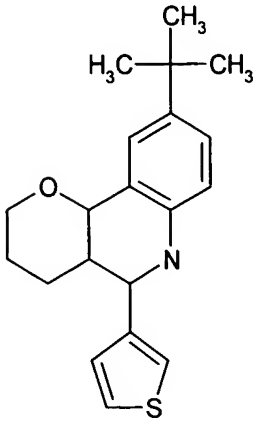

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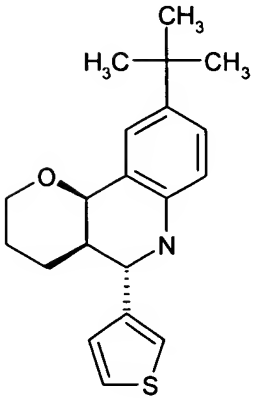

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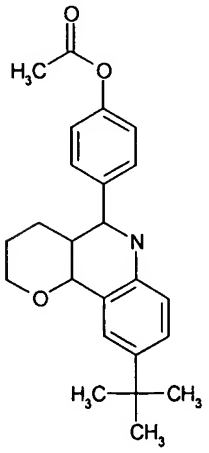

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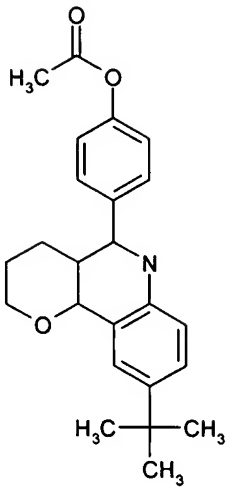

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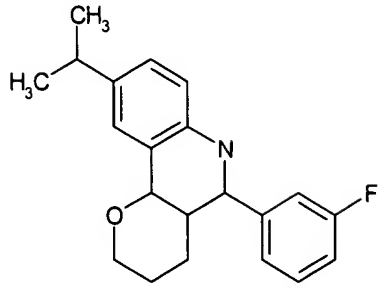

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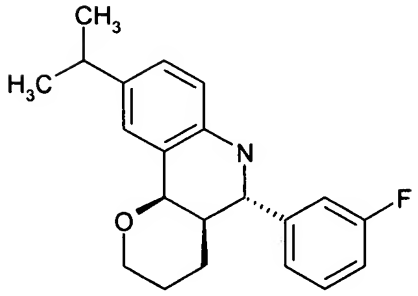

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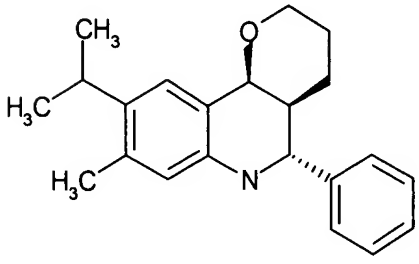

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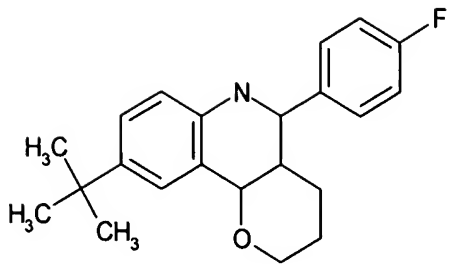

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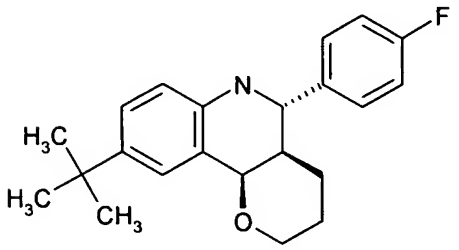
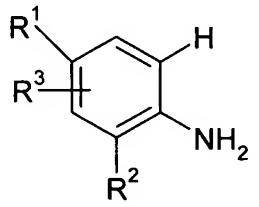


14. Process for the preparation of compounds of the formula I according to Claims 1-13 and pharmaceutically usable derivatives, salts, solvates, tautomers and stereoisomers thereof, characterised in that a compound of the formula II

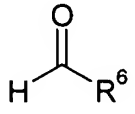


II

,

in which R^1, R^2 and R^3 have the meanings indicated in Claim 1,

is reacted with a compound of the formula III



III

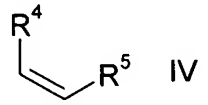
,

in which

R^6 has the meaning indicated in Claim 1,

and

with a compound of the formula IV, the double-bond isomer thereof (E isomer) or mixtures thereof



IV

in which R^4 and R^5 have the meanings indicated in Claim 1,

and, if desired, a radical R^7 which denotes H is converted into a radical R^7 which has a meaning other than H,

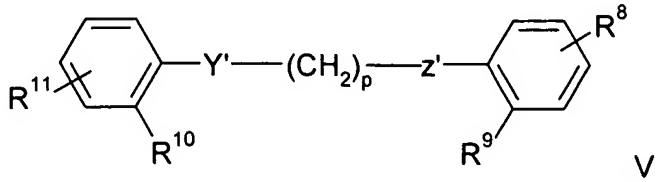
and/or, if desired,
a base or acid of the formula I is converted into one of its salts.

15. Process according to Claim 14, characterised in that the reaction is carried out in the presence of a protonic acid or Lewis acid.

16. Process according to Claim 14 or 15, characterised in that the reaction is carried out in the presence of trifluoroacetic acid, hexafluoroisopropanol, bismuth(III) chloride, ytterbium(III) triflate, scandium(III) triflate or cerium(IV) ammonium nitrate.

17. Medicaments comprising at least one compound of the formula I according to Claim 1 to 13 and/or pharmaceutically usable derivatives, salts, solvates, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

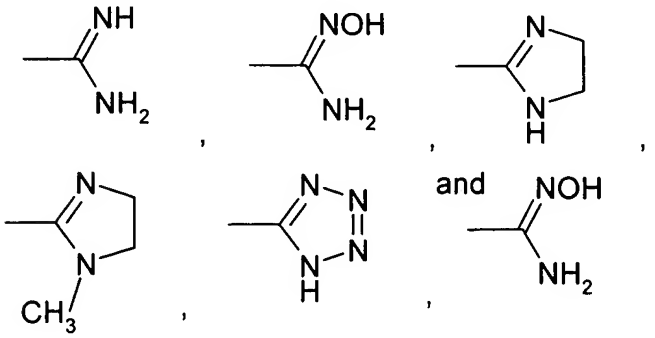
18. Mixture comprise one or more compounds of the formula I and an amount of one or more compounds of the formula V, analogues thereof and/or metabolites thereof



V

in which

Y' and Z' each, independently of one another, denote O or N, R^9 and R^{10} each, independently of one another, denote H, OH, halogen, OC1-10-alkyl, OCF_3, NO_2 or NH_2, n denotes an integer between 2 and 6 inclusive, and R^8 and R^{11} are each, independently of one another, in the meta- or para-position and are selected from the group:



19. Use according to Claim 18, where the compound of the formula V used are pentamidine or salts thereof.

20. Use of compounds according to Claim 1 to 13 and pharmaceutically usable derivatives, salts, solvates, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, or the mixture according to Claim 18, for the preparation of a medicament for the treatment

of diseases which can be influenced by the inhibition, regulation and/or modulation of the mitotic motor protein Eg5.

21. Use of compound according to Claim 1 to 13 or the mixture according to Claim 18 for the preparation of a medicament for the treatment and prophylaxis of cancer diseases.

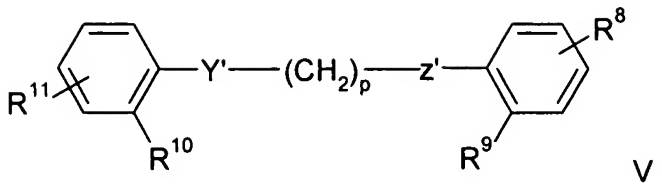
22. Use according to Claim 21, where the cancer diseases are associated with a tumour from the group of tumours of the squamous epithelium, of the bladder, of the stomach, of the kidneys, of head and neck, of the oesophagus, of the cervix, of the thyroid, of the intestine, of the liver, of the brain, of the prostate, of the urogenital tract, of the lymphatic system, of the stomach, of the larynx and/or of the lung.

23. Use according to Claim 22, where the tumour originates from the group monocytic leukaemia, lung adenocarcinoma, small-cell lung carcinomas, pancreatic cancer, glioblastomas and breast carcinoma and colon carcinoma.

24. Use according to Claim 21, where the cancer disease to be treated is a tumour of the blood and immune system.

25. Use according to Claim 24, where the tumour originates from the group acute myelotic leukaemia, chronic myelotic leukaemia, acute lymphatic leukaemia and/or chronic lymphatic leukaemia.

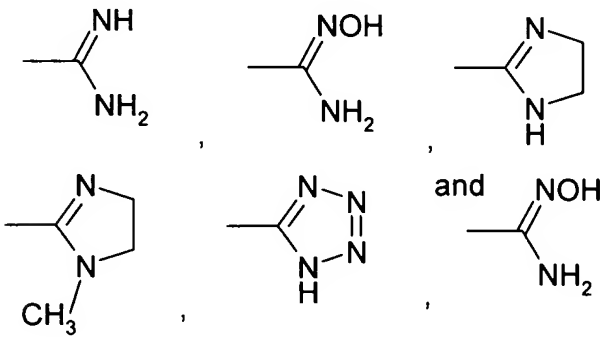
26. Use of compounds of the formula I according to Claim 1 to 13 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of tumours in combination with a therapeutically effective amount of one or more compounds of the formula V, analogues thereof and/or metabolites thereof



V

in which

Y' and Z' each, independently of one another, denote O or N, R^9 and R^{10} each, independently of one another, denote H, OH, halogen, OC1-10-alkyl, OCF_3, NO_2 or NH_2, n denotes an integer between 2 and 6 inclusive, and R^8 and R^{11} are each, independently of one another, in the meta- or para-position and are selected from the group:



where

the compounds of the formula I and the compounds of the formula V, analogues thereof and/or metabolites thereof are administered simultaneously or within 14 days of one another in amounts which are sufficient to inhibit the growth of a tumour or of other hyperproliferative cells.

27. Use according to Claim 26, where the compound of the formula V used are pentamidine or salts thereof.

28. Use of compounds of the formula I according to Claim 1 to 13 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of tumours where a therapeutically effective amount of a compound of the formula I is administered in combination with radiotherapy and a compound from the group 1) oestrogen receptor modulator, 2) androgen receptor modulator, 3) retinoid receptor modulator, 4) cytotoxic agent, 5) antiproliferative agent, 6) prenyl-protein transferase inhibitor, 7) HMG-CoA reductase inhibitor, 8) HIV protease inhibitor, 9) reverse transcriptase inhibitor and 10) further angiogenesis inhibitors.

29. Compounds of the formula I in which Q denotes $CH2R^a$, and R^a has one of the following meanings: NHR_2, NR_2, $NR(CH_2)_n$aryl, $NR(CH_2)_nOR$, COOR, N-pyrrolidone radical, OCOR, $NR(CH_2)_nNR_2$, $N[(CH_2)_nNR_2]CO(CH_2)_n$aryl, $N[(CH_2)_nNHCOOR]$COaryl, R^1, $N[CH_2(CH_2)_nOR]_2$, $NR(CH_2)_nNCOOR$, $X(CH_2)_nX(CH_2)_nXR$, $NR(CH_2)_nX(CH_2)_nOH$, $NR(CH_2)_nO(CH_2)_nOH$, $(CH_2)_n$COOR, $O(CO)NR(CH_2)_nOR$, $O(CO)(CH_2)_nNR_2$, $NR(CH_2)_nNR_2$, $N[(CH_2)_nNR_2]CO(CH_2)_n$aryl, $N[(CH_2)_nXR]CO(CH_2)_n$aryl, $N[(CH_2)_nXR]CO(CH_2)_n$heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_n$heteroaryl, $N[(CH_2)_nNR_2]CO(CH_2)_nR^1$, $N(R)(CH_2)_nN(R)$COOR, $XCOO(CH_2)_nNR_2$, OSO_2A, OSO_2CF_3, OSO_2Ar, $OCONR_2$ or $OCH_2(CH_2)_nNR$.